THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant(s): Berger, A., et al.
Appl. No.: 10/089,658
Conf. No.: 6858
Filed: July 22, 2002
Title: NUTRITIONAL COMPOSITION
Art Unit: 1615
Examiner: N.G. Ebrahim
Docket No.: 112843-044

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' APPEAL BRIEF

Sir:

Appellants submit this Appeal Brief in support of the Notice of Appeal filed on September 25, 2008. This Appeal is taken from the Final Rejection in the Office Action dated March 25, 2008 and the Advisory Action dated September 5, 2008.

I. REAL PARTY IN INTEREST

The real party in interest for the above-identified patent application on Appeal is Nestec, Ltd. by virtue of an Assignment dated July 30, 2002 and recorded at reel 013140, frame 0505 in the United States Patent and Trademark Office.

II. RELATED APPEALS AND INTERFERENCES

Appellants' legal representative and the Assignee of the above-identified patent application do not know of any prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision with respect to the above-identified Appeal.

III. STATUS OF CLAIMS

Claims 1, 3-11, 13-16 and 18-22 are pending in the above-identified patent application. Claims 2, 12, 17 and 23-25 were previously canceled without prejudice or disclaimer. Claims 1, 3-11, 13-16 and 18-22 stand rejected. Therefore, Claims 1, 3-11, 13-16 and 18-22 are being appealed in this Brief. A copy of the appealed claims is included in the Claims Appendix.

IV. STATUS OF AMENDMENTS

A Final Office Action was mailed on March 25, 2008 in which the Examiner maintained rejections of Claim 19 as indefinite and Claims 1, 3-11, 13-16 and 18-22 as obvious. Appellants filed a Response to Final on July 25, 2008, in which Appellants amended Claim 19. An Advisory Action was mailed on September 5, 2008. In the Advisory Action, the Examiner entered the amendment to Claim 19, withdrew the indefiniteness rejection of Claim 19 and maintained the obviousness rejections of Claims 1, 3-11, 13-16 and 18-22. A copy of the Final Office Action and the Advisory Action are attached as Exhibits A and B, respectively, in the Evidence Appendix.

V. SUMMARY OF CLAIMED SUBJECT MATTER

A summary of the invention by way of reference to the specification and/or figures for each of the independent claims is provided as follows:

Independent Claim 1 is directed to a composition for oral administration page 5, lines 24-27), comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) (page 9, lines 6-10) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament (page 8, lines 13-18), wherein the precursor comprises a long chain polyunsaturated fatty acid (LCPUFA) which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds (page 7, lines 3-10), and having a moiety selected from the group consisting of methyl-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno (page 7, lines 16-19), or wherein the precursor is a LCPUFA or derivative thereof of the general formula X:

wherein R is the alkenyl moiety of the LCPUFA of total chain length 16-28 carbon atoms with 2-6 double bonds (page 7, lines 16-19), with the first double bond at the c-1, c-3, c6, c7, c9, c12 position, counting from the non carboxyl (methyl) part of the molecule; and where R" is selected from the group consisting of -H, lower alkyl, -OH, NH_3, and an acid addition salt or complex thereof (page 7, lines 3-10).

Independent Claim 14 is directed to a method for producing a nutritional or therapeutic composition for oral administration (page 5, lines 29-31) comprising the steps of obtaining a therapeutically effective amount of a naturally occurring precursor that is metabolised to a compound having anandamide activity (page 8, lines 13-18), obtaining a steroidal or non-steroidal anti-inflammatory drug (NSAID), and preparing a composition including the precursor and the steroidal or non-steroidal anti-inflammatory drug (NSAID) (page 8, lines 13-18).

Independent Claim 15 is directed to a method of manufacture a composition for the treatment or prevention of an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite,

nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition, skin inflammation and excess nociception (page 6, lines 3-11; page 6, lines 24-30) comprising the steps of preparing a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) (page 9, lines 6-10) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament (page 8, lines 13-18), wherein the precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds (page 7, lines 16-19), and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno (page 7, lines 16-19).

Independent Claim 16 is directed to a method of treating an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite, nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition, skin inflammation and excess nociception (page 6, lines 3-11; page 6, lines 24-30) which comprises administering to a patient having an anandamide-mediated ailment an effective amount of a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) (page 9, lines 6-10) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament (page 8, lines 13-18), wherein the precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds (page 7, lines 16-19), and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno (page 7, lines 16-19).

Although specification citations are given in accordance with C.F.R. 1.192(c), these reference numerals and citations are merely examples of where support may be found in the specification for the terms used in this section of the Brief. There is no intention to suggest in any way that the terms of the claims are limited to the examples in the specification. As demonstrated by the references numerals and citations, the claims are fully supported by the specification as required by law. However, it is improper under the law to read limitations from

the specification into the claims. Pointing out specification support for the claim terminology as is done here to comply with rule 1.192(c) does not in any way limit the scope of the claims to those examples from which they find support. Nor does this exercise provide a mechanism for circumventing the law precluding reading limitations into the claims from the specification. In short, the references numerals and specification citations are not to be construed as claim limitations or in any way used to limit the scope of the claims.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1, 3-11 and 13 are rejected under 35 U.S.C. §103(a) as being unpatentable over "2-Arachidonoyl-glycerol as an 'Endocannabinoid': Limelight for a Formerly Neglected Metabolite," Biochemistry (Mosc.) 63(1):13-21, Jan. 1998, to V. Di Marzo ("*Di Marzo*") in view of U.S. Patent No. 6,552,031 to Burch et al. ("*Burch*"). Copies of *Di Marzo* and *Burch* are attached herewith as Exhibits C and D, respectively, in the Evidence Appendix.

2. Claims 14-22 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Di Marzo* and *Burch* and in further view of WO 94/28913 to Kyle et al. ("*Kyle*"). A copy of *Kyle* is attached herewith as Exhibit E in the Evidence Appendix.

VII. ARGUMENT

A. LEGAL STANDARDS

Obviousness under 35 U.S.C. § 103

The Federal Circuit has held that the legal determination of an obviousness rejection under 35 U.S.C. § 103 is:

> whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made...The foundational facts for the prima facie case of obviousness are: (1) the scope and content of the prior art; (2) the difference between the prior art and the claimed invention; and (3) the level of ordinary skill in the art...Moreover, objective indicia such as commercial success and long felt need are relevant to the determination of obviousness...Thus, each obviousness determination rests on its own facts.

In re Mayne, 41 U.S.P.Q. 2d 1451, 1453 (Fed. Cir. 1997).

In making this determination, the Patent Office has the initial burden of proving a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 U.S.P.Q. 2d 1955, 1956 (Fed. Cir. 1993). This burden may only be overcome "by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings." *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q. 2d 1596, 1598 (Fed. Cir. 1988). "If the examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 24 U.S.P.Q. 2d 1443, 1444 (Fed. Cir. 1992).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference or references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 837 F.2d 1071, 5, U.S.P.Q.2d 1596 (Fed. Cir. 1988). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). Finally, all of the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q., 580 (CCPA 1974).

Further, the Federal Circuit has held that it is "impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the

claimed invention is rendered obvious." *In re Fritch*, 23 U.S.P.Q.2d 1780, 1784 (Fed. Cir. 1992). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988).

Moreover, the Federal Circuit has held that "obvious to try" is not the proper standard under 35 U.S.C. §103. *Ex parte Goldgaber*, 41 U.S.P.Q.2d 1172, 1177 (Fed. Cir. 1996). "An-obvious-to-try situation exists when a general disclosure may pique the scientist curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." *In re Eli Lilly and Co.*, 14 U.S.P.Q.2d 1741, 1743 (Fed. Cir. 1990).

Of course, references must be considered as a whole and those portions teaching against or away from the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

B. THE CLAIMED INVENTION

Independent Claim 1 is directed to a composition for oral administration. The oral composition includes a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament, wherein the precursor comprises a long chain polyunsaturated fatty acid (LCPUFA) which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methyl-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno, or wherein the precursor is a LCPUFA or derivative thereof of the general formula X:

wherein R is the alkenyl moiety of the LCPUFA of total chain length 16-28 carbon atoms with 2-6 double bonds, with the first double bond at the c-1, c-3, c6, c7, c9, c12 position, counting from the non carboxyl (methyl) part of the molecule. R" is selected from the group consisting of -H, lower alkyl, -OH, NH_3, and an acid addition salt or complex thereof.

Independent Claim 14 is directed to a method for producing a nutritional or therapeutic composition for oral administration. The method includes obtaining a therapeutically effective amount of a naturally occurring precursor that is metabolised to a compound having anandamide activity. The method also includes obtaining a steroidal or non-steroidal anti-inflammatory drug (NSAID), and preparing a composition including the precursor and the steroidal or non-steroidal anti-inflammatory drug (NSAID).

Independent Claim 15 is directed to a method of manufacture a composition for the treatment or prevention of an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite, nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition, skin inflammation and excess nociception. The method includes preparing a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament. The precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno.

Independent Claim 16 is directed to a method of treating an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite, nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition,

skin inflammation and excess nociception. The method includes administering to a patient having an anandamide-mediated ailment an effective amount of a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament. The precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno.

C. THE REJECTION OF CLAIMS 1, 3-11 AND 13 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS

Appellants respectfully submit that the obviousness rejection of Claims 1, 3-11 and 13 should be reversed because the Examiner has failed to establish a *prima facie* case of obviousness. In the Office Action, the Examiner alleged that the combination of *Di Marzo* in view of *Burch* renders the claimed subject matter obvious. However, the Examiner fails to establish a *prima facie* case of obviousness because there exists no reason that the skilled artisan would have combined the cited references to arrive at the presently claimed subject matter.

Appellants respectfully submit that there exists no reason why the skilled artisan would combine *Di Marzo* and *Burch* to arrive at the present claims. Because the Examiner admits that *Di Marzo* does not disclose a combination of an anandamide precursor and an NSAID, the Examiner cites *Burch* to cure the deficiencies of *Di Marzo*. The Examiner alleges that *Burch* teaches the combination of oxycodone and rofecoxib, and maintains that it would be "a good motivation to the skilled artisan to replace oxycodone with anandamide as anandamide derivatives and precursors do not have the addictive characteristics of oxycodone." See, Final Office Action, page 5, lines 7-14. However, Appellants respectfully submit that, in contrast to the Examiner's assertion, the skilled artisan would have no reason to replace oxycodone with anandamide to arrive at the present claims.

Opiod analgetics, such as oxycodone, may be deployed as a substitute for heroin or morphine, and can result in similar negative side-effects. For example, opiod analgetics can be

extremely addictive to the user and can result in adverse reactions including miosis, perspiration, dysphoria, sedation, pururitus, obstipation, respiratory depression, orthostatic hypotention, hallucinations, hyperalgesia, delirium, induction of tolerance etc. Opiod analgetics may also cause side effects that include severe nausea, which, in fact, is known to be treated by the use of cannabinoids or cannabimimetic substances. Oxycodone, in particular, is a controlled substance in the United States both as a single agent and in combination with products containing paracetamol, or ibuprofen or aspirin (NSAIDs).

In contrast, the use of an anandamide, a naturally occurring neutransmitter found in the human body, in conjunction with NSAID's provides the synergistic advantage of the combination without, or with fewer, detrimental side effects than certain drugs, including opiod analgetics. However, opiod analgetics and antimimetics (anandamide) comprise pharmaceutically different effective groups characterized by different mechanisms of action. The two systems not only bring about different side effects both in terms of quality and quantity, as discussed above, but also utilize different ligands and receptors in their respective mechanisms of action.

For example, oxycodone (an opiod analgetic) acts as a weak agonist at mu, kappa, and delta opioid receptors within the central nervous system (CNS). Oxycodone primarily affects mu-type opioid receptors, which are coupled with G-protein receptors and function as modulators, both positive and negative, of synaptic transmission via G-proteins that activate effector proteins. Binding of the opiate stimulates the exchange of GTP for GDP on the G-protein complex. As the effector system is adenylate cyclase and cAMP located at the inner surface of the plasma membrane, opioids decrease intracellular cAMP by inhibiting adenylate cyclase. Subsequently, the release of nociceptive neurotransmitters such as substance P, GABA, dopamine, acetylcholine, and noradrenaline is inhibited. Opioids such as oxycodone also inhibit the release of vasopressin, somatostatin, insulin, and glucagon. Opioids close N-type voltage-operated calcium channels (kappa-receptor agonist) and open calcium-dependent inwardly rectifying potassium channels (mu and delta receptor agonist). See, http://www.drugbank.ca/drugs/DB00497.

In contrast, anandamides are mediated primarily by cannabinoid receptors. Cannabinoid receptors are part of the largest known family of receptors which have distinctive patterns in which the receptor molecule spans the cell membrane seven times over. There are currently two

known types of cannabinoid receptors, CB1 and CB2. CB1 receptors are found primarily in the brain, specifically in the basal ganglia and in the limbic system, including the hippocampus. They are also found in the cerebellum and in both male and female reproductive systems. CB1 receptors are essentially absent in the medulla oblongata, the part of the brain stem that is responsible for respiratory and cardiovascular functions. Thus, there is not a risk of respiratory or cardiovascular failure with the use of anandamides as there is with many other drugs. CB2 receptors are almost exclusively found in the immune system, with the greatest density in the spleen. While generally found only in the peripheral nervous system, a report does indicate that CB2 is expressed by a subpopulation of microglia in the human cerebellum. http://en.wikipedia.org/wiki/Anandamide.

In this regard, Appellants respectfully submit that if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). This certainly applies here where the opiod analgetics and antimimetics (anandamide) comprise pharmaceutically different effective groups characterized by different mechanisms of action and utilize different ligands and receptors in their respective mechanisms of action, as discussed above.

Accordingly, and in contrast to the Examiner's repeated assertions, Appellants respectfully submit that the skilled artisan would have no reason to replace oxycodone (an opiod analgetic) with an anandamide to arrive at the present claims.

Moreover, Appellants also respectfully submit that each reference must be considered as a whole and those portions teaching against or away from each other and/or the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). "A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant." *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

In its attempt to arrive at the present claims by combining the cited references, the Examiner has ignored significant portions of each reference that teach away from the combination. For example, *Burch* specifically teaches away from the claimed subject matter

when *Burch* teaches that a COX-2 inhibitor (such as rofecoxib) "would have advantages over NSAID'S." See, *Burch*, col. 3, lines 58-60. Appellants respectfully submit that this disclosure of *Burch* would actually lead the skilled artisan in a direction divergent from the path that was taken by Appellants in the present disclosure. *In re Haruna*, 249 F.3d 1327 (Fed. Cir. 2001). See, also, MPEP 1504.03.

Further, the Examiner has improperly applied hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses. In fact, in the instant situation, the prior art provides no teaching or suggestion of the desirability of the modification. Specifically, *Burch* provides no incentive to use any pharmacological system other than the opiod system. The fact that the prior art *may* be modified in the manner suggested by the Examiner does not make the modification obvious. As a result, one having ordinary skill in the art would have no reason to combine the cited references to arrive at the present claims.

Accordingly, Appellants respectfully submit that the skilled artisan would have no reason to combine the cited references to arrive at Claims 1, 3-11 and 13.

For the reasons discussed above, Appellants respectfully submit that Claims 1, 3-11 and 13 are novel, nonobvious and distinguishable from the cited reference.

Accordingly, Appellants respectfully request that the rejection of Claims 1, 3-11 and 13 under 35 U.S.C. §103(a) be withdrawn.

D. THE REJECTION OF CLAIMS 14-22 UNDER 35 U.S.C. §103(a) SHOULD BE REVERSED BECAUSE THE EXAMINER HAS FAILED TO ESTABLISH A *PRIMA FACIE* CASE OF OBVIOUSNESS

Appellants respectfully submit that the obviousness rejection of Claims 14-22 should be reversed because the Examiner has failed to establish a *prima facie* case of obviousness. In the Final Office Action, the Examiner alleged that the combination of *Di Marzo* and *Burch* in view of *Kyle* renders the claimed subject matter obvious. However, the Examiner fails to establish a *prima facie* case of obviousness because *Kyle* fails to remedy the deficiencies of *Di Marzo* and *Burch*.

Appellants respectfully submit that, for many of the same reasons presented above, the combination of *Di Marzo* in view of *Burch* and in further view of *Kyle* is also improper. For example, *Kyle* is entirely directed toward methods and pharmaceutical compositions for treating neurological disorders, wherein the compositions include arachidonic acid, docosahexanoic acid or a combination of both. See, *Kyle*, Abstract. *Kyle* provides no incentive to combine the arachidonic acid or docosahexanoic acids with a steroidal or non-steroidal anti-inflammatory drug (NSAID) to arrive at the present claims.

Moreover, Appellants respectfully submit that simply because *Kyle* is directed, in part, toward the treatment of a neurological disorder using arachidonic acid, this does not make the combination with *Di Marzo* and *Burch* proper. In fact, what the Examiner has done here is to apply hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses. Appellants respectfully submit that if it is proper for the Examiner to combine any number of references to arrive at the present claims simply because each reference suggests an element of the present claims, then every invention would effectively be rendered obvious. Instead, the skilled artisan must have a reason to combine the cited references to arrive at the present claims. Appellants respectfully submit that such a reason is not present in the instant case.

For at least the reasons discussed above, the combinations of *Di Marzo* in view of *Burch*, and *Di Marzo* in view of *Burch* and in further view of *Kyle* fail to render the claimed subject matter obvious.

Accordingly, Appellants respectfully request that the rejection of Claims 14-22 under 35 U.S.C. §103(a) be withdrawn.

For at least the foregoing reasons, Appellants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same.

VIII. CONCLUSION

Appellants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness under 35 U.S.C. §103 with respect to the rejections of Claims 1, 3-11, 13-16 and 18-22. Accordingly, Appellants respectfully submit that the obviousness rejections are erroneous in law and in fact and should therefore be reversed by this Board.

The Director is authorized to charge $540.00 for the Appeal Brief and any additional fees which may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112843-44 on the account statement.

Respectfully submitted,

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Dated: December 19, 2008

CLAIMS APPENDIX

PENDING CLAIMS ON APPEAL OF U.S. PATENT APPLICATION SERIAL NO. 10/089,658

1. A composition for oral administration, comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament, wherein the precursor comprises a long chain polyunsaturated fatty acid (LCPUFA) which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methyl-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno, or wherein the precursor is a LCPUFA or derivative thereof of the general formula X:

wherein R is the alkenyl moiety of the LCPUFA of total chain length 16-28 carbon atoms with 2-6 double bonds, with the first double bond at the c-1, c-3, c6, c7, c9, c12 position, counting from the non carboxyl (methyl) part of the molecule; and where R" is selected from the group consisting of -H, lower alkyl, -OH, NH_3, and an acid addition salt or complex thereof.

3. A composition according to claim 1 wherein the precursor comprises a molecule having a plurality of formula X.

4. A composition according to claim 1 wherein the precursor comprises a molecule having from 1 to 3 copies of formula X esterified to a glycerol backbone; in a sterochemical configuration selected from the group consisting of: *sn*-1,2,3; *sn*-1,2; *sn*-1,3; *sn*-2,3; *sn*-1; *sn*-2; and *sn*-3.

5. A composition according to claim 1 wherein the precursor comprises a fatty acid selected from the group consisting of arachidonate (20:4n-6 AA), linolenate (18:3n-6), gamma linolenate (18:3n-6), dihomogamma-linolenate (30:3n-6 DGLA), adrenic acid (22:4n-6), linolenate (18:3n-3), stearidonic (18:4n-3), eicosatetraenoic (20:4n-3), eicosapentaenoate (20:5n-3), docosahexaenoate (22:6n-3DHA), docosapentaenoate (22:5n-3 or 22:5n-6), tetracosapentaenoate (24:5n-3 or 24:5n-6), tetracosahexaenoate (24:6n-3) and Mead acid (30:3n-9).

6. A composition according to claim 1 wherein the precursor comprises arachidonate (20:4n-6 AA).

7. A composition according to claim 1 which comprises an inhibitor of an anandamide inactivating enzyme (amidase).

8. A composition according to claim 7 wherein the inhibitor is selected from the group consisting of oleate and oleamide, palmitate, palmitoylethanolamide, linoleylethanolamide, 2 palmitoylglycerol, and 2-linoleylglycerol.

9. A composition according to claim 7 wherein the inhibitor is palmitate or palmitoylethanolamide.

10. A composition according to claim 1 which comprises a triacylglycerol having palmitate and arachidonate attached to its backbone wherein arachidonate is at the *sn*-1 and *sn*-2 positions.

11. A composition according to claim 1 which comprises a compound which reacts with a CB receptor.

13. A composition according to claim 1 which comprises a physiologically acceptable carrier, diluent or adjuvant.

14. A method for producing a nutritional or therapeutic composition for oral administration comprising the steps of obtaining a therapeutically effective amount of a naturally occurring precursor that is metabolised to a compound having anandamide activity, obtaining a steroidal or non-steroidal anti-inflammatory drug (NSAID), and preparing a composition including the precursor and the steroidal or non-steroidal anti-inflammatory drug (NSAID).

15. A method of manufacture a composition for the treatment or prevention of an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite, nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition, skin inflammation and excess nociception comprising the steps of preparing a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament, wherein the precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno.

16. A method of treating an anandamide-mediated ailment selected from the group consisting of hypertension, glaucoma, insomnia, pain, inflammation, migraine headaches, loss of appetite, nausia, cramps, diarrhoea, gut upsets, intestinal motility disturbances, asthma, nervousness, catalepsy, low mood, depression, spasms, tics, excessive stress, spasticity, multiple sclerosis and vocalization, poor language acquisition, skin inflammation and excess nociception which comprises administering to a patient having an anandamide-mediated ailment an effective amount of a composition comprising a steroidal or non-steroidal anti-inflammatory drug (NSAID) and a naturally occurring precursor that is metabolised to a compound having anandamide activity for use as a medicament, wherein the precursor comprises an LCPUFA which is a polyunsaturated fatty acid of 16-28 carbon atoms having from 2 to 6 double bonds, and having a moiety selected from the group consisting of methylated-, branched-, cyclic-, conjugated-, non-methylene interrupted-, epoxy-, furanoid-, hydroxyl-, allylic-, trans-, and seleno.

18. A method of claim 14 wherein the method includes the step of purifying the naturally occurring precursor.

19. A method of claim 14 wherein the naturally occurring precursor is synthesized.

20. A method according to claim 16 wherein the precursor is a long chain polyunsaturated fatty acid (LCPUFA) or derivative thereof of the general formula X:

wherein R is the alkenyl moiety of a LCPUFA of total chain length 16-28 carbon atoms with 2-6 double bonds, with the first double bond at the c-1, c-3, c6, c7, c9, c12 position, counting from the non carboxyl (methyl) part of the molecule; and where R" is selected from the group consisting of -H, lower alkyl, -OH, NH_3, and an acid addition salt or complex thereof.

21. A method according to claim 16 wherein the precursor comprises a molecule having from 1 to 3 copies of formula X esterified to a glycerol backbone; in a sterochemical configuration selected from the group consisting of: *sn*-1,2,3; *sn*-1,2; *sn*-1,3; *sn*-2,3; *sn*-1; *sn*-2; and *sn*-3.

22. A method according to claim 16 wherein the precursor comprises a fatty acid selected from the group consisting of arachidonate (20:4n-6 AA), linoleate (18:3n-6), gamma linolenate (18:3n-6), dihomogamma-linolenate (30:3n-6 DGLA), adrenic acid (22:4n-6), linolenate (18:3n-3), stearidonic (18:4n-3), eicosatetraenoic (20:4n-3), eicosapentaenoate (20:5n-3), docosahexaenoate (22:6n-3DHA), docosapentaenoate (22:5n-3 or 22:5n-6), tetracosapentaenoate (24:5n-3 or 24:5n-6), tetracosahexaenoate (24:6n-3) and Mead acid (30:3n-9).

EVIDENCE APPENDIX

EXHIBIT A: Final Office Action dated March 25, 2008

EXHIBIT B: Advisory Action dated September 5, 2008

EXHIBIT C: "2-Arachidonoyl-glycerol as an 'Endocannabinoid': Limelight for a Formerly Neglected Metabolite," Biochemistry (Mosc.) 63(1):13-21, Jan. 1998, to V. Di Marzo (*"Di Marzo"*), cited by the Examiner in the Office Action dated March 25, 2008

EXHIBIT D: U.S. Patent No. 6,552,031 to Burch et al (*"Burch"*), cited by the Examiner in the Office Action dated March 25, 2008

EXHIBIT E WO 94/28913 to Kyle et al (*"Kyle"*), cited by the Examiner in the Office Action dated March 25, 2008

RELATED PROCEEDINGS APPENDIX

None.